## REMARKS

Reconsideration of the application in light of the amendments and the following remarks is respectfully requested.

### Status of the Claims

Claims 9 and 24 have been amended to depend from claims 1 and 17, respectively. Claim 17 has been amended to recite that the atorvastatin layer includes a stabilizer. Support for this amendment can be found, for example, at p. 2, ll. 18-22; p. 4, ll. 25-31; p. 5, ll. 3-7; p. 8, ll. 1-6 and 24-35 and Example 3 of the application, as filed. No new matter has been added by this amendment. Claims 1-7 and 9-49 are currently pending in this application. As claims 11, 12, 19-23, 32-35, 47 and 49 have been withdrawn from consideration, only claims 1-7, 9-10, 13-18, 24-31, 36-46 and 48 are at issue.

### Objections to the Claims

Claim 9 is objected to because it depends on a canceled claim (claim 8). Applicants have amended claim 9 to depend from claim 1. Accordingly, Applicants respectfully request withdrawal of this objection.

### Obviousness Rejections

Claims 1-7, 9-10, 13-18, 24-31, 36-46 and 48 remain rejected as obvious over U.S. Patent No. 6,534,088 ("Guivarc'h") in view of U.S. Patent Publication No. 2005/0148594 ("Cink"), as evidenced by MeSH Descriptor Data, 2007 ("MeSH"). The Examiner contends that Guivarc'h teaches a coated tablet comprising a fenofibrate stabilized by a phospholipid, and a statin (Office Action, p. 3). In the Examiner's view, Cink teaches a formulation of fenofibrate and a stabilizer (tromethamine) and optionally, atorvastatin (Office Action, p. 4). According to the Examiner, MeSH discloses that tromethamine is also referred to as 2-amino-2-(hydroxymethyl)-1,3-propanediol. The Examiner argues that it would have been obvious to combine the teachings of Guivarc'h and Cink to arrive at the present invention (Office Action, p. 4).

Applicants respectfully traverse this rejection, and request reconsideration.

The Examiner argues it would have been obvious to combine Guivarc'h and Cink (Office Action, p. 4). However, this combination would not have led the ordinary skilled artisan to the composition called for by the present claims. Instead, at best, the combination of references would have led the ordinary skilled artisan to a composition with the active agents in a single layer, together with a film or enteric coating (*see* Guivarc'h, col. 46). Additionally, even if for argument's sake Guivarc'h suggests a composition with the two active ingredients in separate layers, Cink does not teach or disclose the stabilization of atorvastatin with tromethamine. Instead, Cink teaches tromethamine salts of fenofibrate. There is no suggestion to include tromethamine in the atorvastatin layer. Therefore, the Examiner has not met her burden of establishing a *prima facie* case of obviousness.

In response to the argument that neither Cink nor Guivarc'h teach a tablet with separate active agent layers (set forth in the July 6, 2009 Amendment), the Examiner states that "Applicant is guided above to teachings of multi-layer compositions" (Office Action, p. 6). The disclosure of enteric coatings in Guivarc'h would not have led one of ordinary skill in the art to formulate an active ingredient in the enteric coating layer. Instead, the ordinary skilled chemist would have recognized that an enteric coating is employed to prevent digestion of the active ingredient layer. It would defeat the purpose of the enteric coating if the active ingredient was in this layer, because the enteric coating is present as a barrier, to prevent digestion of the active ingredient. For at least this reason, Guivarc'h would not have led the ordinary skilled artisan to formulate two active ingredients in separate layers of a composition.

Furthermore, there is no suggestion in Guivarc'h to formulate two active agents in two different layers. Guivarc'h teaches that administration of separate formulations of a statin and fenofibrate resulted in a food effect (Guivarc'h, col. 12, ll. 17-20, 28-31, 39-41). Further, Guivarc'h teaches that when the statin is insoluble or poorly soluble in water, it can either (1) be micronized in the presence of a phospholipid, and mixed with the suspension of fenofibrate; or (2) co-suspended and co-micronized in the presence of a phospholipid (Guivarc'h, col. 16, ll. 27-40). Upon

considering these teachings, the skilled artisan would not have formulated atorvastatin and fenofibrate in separate layers. Instead, assuming for argument's sake that a statin and fenofibrate were to be combined, the skilled artisan would have formulated both active ingredients together, in a single layer. The Examiner has not provided any rationale as to why the ordinary skilled artisan would have gone against the teachings of Guivarc'h, and make a composition having a statin and fenofibrate in separate layers.

Neither Cink nor MeSH cures this deficiency, as neither suggest a two layer formulation, with the active agents in separate layers.

Futhermore, Cink does not teach tromethamine as a stabilizer for a statin in a composition comprising fenofibrate and a statin (HMG–CoA reductase inhibitor) in separate layers, as recited in claim 26. Cink discloses a tromethamine salt of fenofibrate (*see*, *e.g.*, Example 27). Since fenofibrate and the HMG–CoA reductase inhibitor are present in separate layers in the presently claimed composition, tromethamine in the fenofibrate layer would not interact with the HMG-CoA reductase inhibitor (the statin). Therefore, Cink does not disclose or suggest the subject matter called for by the pending claims, either alone, or in combination with Guivarc'h.

None of the cited references disclose or suggest a stable composition containing both fenofibrate and an HMG-CoA reductase inhibitor, in separate layers. A separate layer composition provides superior HMG-CoA reductase inhibitor stability, as compared to a composition with both active ingredients in the same layer. As shown by Example 6, simvastatin is not stable when present in a single layer tablet with fenofibrate. In particular, 3.9% of the simvastatin converted to its corresponding hydroxy acid when simvastatin granules were mixed with fenofibrate granules, tabletted, and stored for 1 month at 25°C and 60% relative humidity. In contrast, when the simvastatin and fenofibrate granules were incorporated into separate layers in a tablet, only 0.2% of the simvastatin converted to its hydroxy acid under the same conditions (a 19.5 times improvement in stability). The presently claimed composition, therefore, provides superior HMG-CoA reductase inhibitor stability. This enhanced stability is not disclosed or suggested by the cited references.

For at least the reasons given above, Applicants respectfully request withdrawal of this rejection.

Claims 17, 18 and 37 also remain rejected as obvious over Guivarc'h in view of Cink, as evidenced by MeSH Descriptor Data, 2007, as applied to claims 1-10, 13-16, 24-31, 36 and 38-46 above, and further in view of U.S. Patent Publication No. 2004/0023919 ("Ohsawa"). Guivarc'h, Cink and MeSH are discussed above. Applicants note that this rejection was reiterated verbatim from the previous Office Action, and that the Examiner has not responded to the arguments presented in the February 9, 2009 Amendment.

Although Ohsawa teaches ascorbic acid in an atorvastatin formulation, Ohsawa does not cure the deficiencies of the combination of Guivarc'h, Cink and MeSH, as discussed above. Specifically, Ohsawa does not disclose or suggest a formulation containing separate layers for fenofibrate and atorvastatin. Therefore, the pending claims are not obvious over these references.

Ohsawa teaches that ascorbic acid co-administration with atorvastatin reduces total cholesterol levels. Pending claims 17 and 18 call for a stabilizer capable of providing a microenvironment for atorvastatin having a pH of at least about 5 or 6. A 5% solution of ascorbic acid has a pH of about 2.5. Therefore, ascorbic acid is not a stabilizer that can provide a microenvironment for atorvastatin having a pH of at least about 5 or 6.

For at least the reasons given above, Applicants request withdrawal of this obviousness rejection, and reconsideration of the claims.

## CONCLUSION

Based on the preceding amendments and arguments, the pending claims are believed to be in condition for allowance, which is earnestly solicited. If there are remaining issues that the Examiner believes could be addressed by conducting an interview or entering an Examiner's Amendment, the Examiner is cordially invited to contact the undersigned agent to discuss such issues.

Dated: March 1, 2010

Respectfully submitted,

By _____

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